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REACTIONS, IN HUMAN PATIENTS, RESULTING FROM INFUSION OF SPECIES NONSPECIFIC SERUM

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In 1943, N. G. Belen'kiy succeeded in freeing cattle serum from primary toxic and anaphylactic effects (by primary toxic effects are meant effects which are observed at the time of the first infusion). His experimental work formed a basis for application of the new serum, called species nonspecific by its originator, for therapeutic purposes at clinics of the Institute imeni Sklifosovskiy (cf work by D. A. Arapov). The serum was administered in surgical conditions, mainly as a substitute for human plasma. One of the aims of administering the serum was parenteral feeding.

Because toxic and anaphylactic properties of the serum could only express themselves clinically in the form of reactions exhibited by the patients, we watched the patients for these reactions. In appended Table 1 we indicate the dependence of the reactions on the doses of serum which had been administered. The results listed in the table show that the number of reactions decreases with increased doses of the serum. This indicates that Belen'kiy's serum actually does not have any toxic properties, otherwise an increase of the dosis would necessarily result in an increase in the number of reactions. The greatest number of reactions corresponds to small doses, because appearance of reactions of medium and high intensity induced us to stop the infusion at an early stage.

The clinical aspects of the reactions were multiform and the intensity of the reaction varied. All reactions were arbitrarily subdivided, according to the intensity of the process, into three categories and referred to as light, medium, and acute reactions.

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The symptoms of the light reaction consist of a headache, pains in the waist and along the course of the vein starting at the site of the injection, difficulty in breathing, hyperemia of the face, and a light chill and shivering. All these symptoms arise during the infusion after 5-10 cu cm have been introduced and have a transitory character. It is sufficient to interrupt the flow of serum for 3-5 min by compressing the rubber tube to make these symptoms disappear. They then pass and are not renewed. The infusion can then be generally completed.

In the case of a medium reaction, there is a light chill which occasionally becomes strong. Further symptoms are hyperemia of the face, pains in the chest, and acceleration of the pulse up to 100 beats per minute. This type of reaction appears 3-5 min after the beginning of the infusion. Upon compression of the rubber tube, this type of reaction may cease in 5-6 min and then not recur when the infusion is continued. This occurs rarely, however, in the majority of cases the reaction sets in again when infusion is renewed. Consequently, one must make it a rule to stop administering serum at this stage of the reaction. The acute reaction manifests itself by the same symptoms as the reaction of medium intensity. However, these symptoms are accompanied by a sharp acceleration of the pulse and respiration (120:30), as well as a drop in the blood pressure.

A female patient, 62 years old, was to be operated on for a tumor of the esophagus. Because the patient was considerably debilitated, administration of species nonspecific serum was begun. Upon introduction of 100 cu cm of the serum (on the 9th and 10th min), the patient began to complain of difficulty in breathing and of a chill. At this stage, the pulse was frequent and weak and the blood pressure had dropped to 70/50 mm. Lobeline, camphor, and oxygen were thereupon administered to the patient. After several minutes, the pulse became slower and stronger. Fifteen minutes after the beginning of the reaction the patient felt quite well. The pulse (80 beats per min) was even and of full strength.

The above gives a brief characterization of the reactions of the sick organism to introduction of species nonspecific serum. The frequency distribution was as follows: among 79 reactions, 48 were light, 15 medium, and 16 acute. The majority of reactions turned out to be light and were encountered at high dosages; strong reactions occurred in the group of patients who had received up to 100 cu cm of serum. On repeated administration of the serum, reactions were encountered in 19 cases. Fourteen of these cases presented the same clinical picture observed at the first introduction of the serum: there was no itching or rash, i.e., no late symptoms of serum sickness. Consequently, the reactions in these cases must be regarded as toxic. As far as the remaining five reactions are concerned, four of them set in as a result of a repeated infusion carried out on the 4th to 5th day after the first infusion. Here the reactions consisted of a rash of the urticaria type, which disappeared rapidly, and an itching of the skin which continued for 30 minutes.

Acute symptoms of serum sickness occurred only on one occasion, on the 8th day after the first infusion of species nonspecific serum, but this did not indicate any anaphylaxis-producing properties of the serum, because the patient developed the same condition a year earlier after transfusion of donor blood. We happened to encounter in this instance a typical case of individual protein intolerance.

Repeated infusions were carried out on the next day, as well as on the 2d to 20th day after the first administration. The most typical example of the absence of anaphylactic reaction was a female patient who was admitted to the clinic for treatment of high blood pressure with species nonspecific serum. The serum was administered to this patient /without ill effects/ 54 times during a 6-month period at intervals of 1-10 days.

The general characteristics of the reactions were that they set in during the process of infusion, as well as their brevity and mildness. One to 2 hours after the onset of a severe reaction, the majority of patients felt quite well; they had a good appetite and even expressed a desire to get out of bed.

Our observations have led to the conclusion that species nonspecific serum does not exert any primary toxic or anaphylactic effects. If the serum had toxic properties, an increase of the dosis would lead to an increase in the number of reactions and also would increase their intensity. If the serum had anaphylaxis-producing properties, an increase in the number of infusions would inevitably lead to an anaphylactic shock. Neither has been observed. The majority of reactions corresponds precisely to doses which were administered more frequently than any of the others. Some patients received 1.5 or 2.1 /cubic centimeters?/ of the serum per day during a week, for the purpose of parenteral feeding, and no reactions occurred. Because repeated infusions did not lead to anaphylactic reactions, one must conclude that species nonspecific serum is no. anaphylactogenic.

Since factory production of the serum has been started only recently, the batches are not quite uniform in quality; some of them are more toxic than the others. However, in a certain percentage of cases (no less than 6%), reactions resulting from administration of species nonspecific serum take place independently of the quality of the product. The reactions are of the colloidoclastic type and are due to individual protein intolerance /literally incompatibility/. This assumption is confirmed in that in some cases transfusion of donor blood induces a reaction, while a subsequent infusion of species nonspecific serum does not.

We have purposely emphasized the drawbacks of species nonspecific serum, because this is a new preparation. However, the experience acquired on 1,000 treatments shows that species nonspecific serum has a powerful hemodynamic, replacing, detoxifying, and stimulating action which is not inferior to that of human plasma. The possibility of utilizing species nonspecific serum as a source of parenteral protein nutrition is extremely important; it opens up a new era in surgical treatment. Our studies have established that protein introduced in this manner is completely taken up by the human organism.

CONCLUSIONS

1. Species nonspecific serum is devoid of primary toxic and anaphylactogenic properties.

2. The percentage of reactions resulting from the infusion of species nonspecific serum is at the approximate level of ten. The infusions do not give rise to complications.

3. The size of the dosis has no effect on the type and intensity of the reaction.

4. Species nonspecific serum may be administered repeatedly after any desired interval of time.

5. Species nonspecific serum has a replacing, detoxifying, and stimulating action. It is a substitute for human plasma in these respects.

6. One must note the value of species nonspecific serum as an agent supplying parenteral protein nutrition.

/Appended table follows./

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Table 1. Effect of Dosage of Species Nonspecific Serum on the Number of Primary Reactions

Dosis (cu cm)	No of Infusions	No of Reactions
Up to 100	143	31
250	285	29
500	386	14
750	46	2
1,000	91	2
1,500	25	-
2,000	19	-
2,500	1	-
3,000	3	1
4,000	1	-
Total	1,000	79

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